

Appl. No.: 09/957,446
Amdt. dated 08/22/2005
Reply to Office action of June 15, 2005

REMARKS/ARGUMENTS

In light of the amendments to the claims presented herein and the following remarks, reexamination and reconsideration of this application, withdrawal of the rejections, and formal notification of the allowability of all claims as presented are earnestly solicited. As detailed in the Office Action mailed June 15, 2005, Claims 1-90 are pending, wherein Claims 1-90 have been rejected. In response to the Office Action, Claims 1, 14, 41-55, 66, and 77-90 have been amended. The amendments to the claims find support throughout the Specification and the Drawings and no new matter has been added. Accordingly, it is believed that the claims now define patentable subject matter over the prior art cited in the Office Action and notice to such effect is requested at the Examiner's earliest convenience.

Claim Objections

Claim 66 was objected to in the Office Action for informalities. In response, Claim 66 has been amended as suggested in the Office Action. Accordingly, the Applicants submit that this rejection is now moot.

Claim Rejections – 35 U.S.C. §101

Claims 41-54 and 77-90 were rejected in the Office Action as being directed to non-statutory subject matter. In response, Claims 41-54 and 77-90 have been amended to indicate that the claimed subject matter is directed to a "computer-readable medium encoded with a computer program," as suggested in the Office Action. Accordingly, the Applicants submit that these rejections are now moot and request withdrawal of the same.

Claim Rejections – 35 U.S.C. §103

Claims 1, 11, 14, 26-28, 36-38, 41, 42, 50-52, 55, 64-66, 72-74, 77, 78, and 86-88 were rejected in the Office Action as being obvious over U.S. Patent No. 4,997,769 to Lundsgaard in view of U.S. Patent No. 5,835,617 to Ohta *et al.* The Applicants respectfully traverse these rejections. However, the Applicants have amended Claims 1, 14, 41, 55, and 77 to further clarify

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the subject matter being claimed. These amendments find support throughout the Specification and the Drawings and no new matter has been added.

The Lundsgaard '769 patent discloses a method and apparatus for determining oxygen saturation or oxygen content of a blood sample by determining a total of five hemoglobin derivatives. The apparatus 10 includes a conduit system comprising an inlet tube 11 extending from an aperture 12 at an outer side surface of the housing of the apparatus to a hemolyzing and measuring block 13 and further to a liquid detector and liquid conduit divider block 14, in which a liquid detector 28 is arranged. Below the lower side surface of the hemolyzing and measuring block 13, a light emitting device 35 constituted by a photo lamp is arranged. The intensity of the light emitted from the light emitting device 35 is detected by a light detector 101 constituted by a photodiode. The light detector is connected to a control circuit which supplies power to the light emitting device 35 and serves the purpose of maintaining a constant intensity of light radiated from the light emitting device 35. Part of the light emitted from the light emitting device or photo lamp 35 is transmitted through the blood sample contained in a cuvette 67 which constitutes part of the conduit extending through the hemolyzing and measuring block 13 and is optically processed in a monochromator assembly 36. Measuring signals generated in the monochromator assembly 36 are input to a signal processor 37 which further communicates with a central microcomputer 38 in which the measuring signals generated in the monochromator assembly 36 are processed. In the signal processor 37 are further processed.

The Lundsgaard '769 patent further discloses that the optical system of the monochromator assembly 36 comprises an input part 47 for transmitting light from the light emitting device or photo lamp 35 to the blood sample contained in the cuvette 67 of the hemolyzing and measuring block 13, and an output part 48 for guiding or transmitting light transmitted through the blood sample contained in the cuvette 67 of the block 13 to a plurality of light detectors. The output part 48 comprises a biconvex lens 53, an optical screening device 54 having an aperture aligned in relation to the light transmission path of the biconvex lens, the block 13 and the input part 47, and further a concave mirror 57 and an optical grating device 58. From the aperture 55 of the optical screening device 54 the light is transmitted to the

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concave mirror 57 and further to the optical grating device 58 for separating the light transmitted to the grating device into monochromatic components. The light transmitted from the concave mirror 57 to the optical grating device 58, where part of the light transmitted to the optical grating device 58 is re-transmitted to the concave mirror 57 to the screening device 54. The screening device 54 is a plane and hollow device in which a plurality of light detectors or photodiodes 62 is housed. The individual light detectors or photodiodes 62 are exposed to monochromatic or substantially monochromatic light separated in the grating device 58 and reflected from the concave mirror 57 through slits or apertures 63 of the front surface of the screening device 54 facing the concave mirror 57. The light detectors or photodiodes 62 are constituted by photodiodes sensitive to light of a wavelength of approximately 400 nm-1000 nm and generate photodiode currents of the order of 1-400 nA. The logarithmic amplifier converts the photodiode current to 4 V/dec; 0 V=1 μ A. The outputs of the logarithmic amplifier 92 is converted to a normalized measuring signal representing the light intensities detected by the photodiodes 62 are input to an analog/digital converter 97. The output of the analog/digital converter 97 is connected to an interface input/output block 98 the output of which is connected to a bus 88.

The Ohta '617 patent discloses an arithmetic control mechanism of an optical CT apparatus for providing a tomographic image that calculates first light densities in output portions of an object on the basis of a numerical analysis method, when it is assumed that the object is divided into fine segments and all segments have the same value as an absorption coefficient under predetermined conditions equivalent to an actual measurement; and calculates second light densities in the output portions, when it is assumed that sequentially selected one of the segments has a specific value as an absorption coefficient under the predetermined conditions. Further, the mechanism calculates, as influences of the segments, ratios of the first to the second light densities, thereby obtaining an influence matrix corresponding to an arrangement of the segments; calculates relative ratios of the third light densities in the output portions on the basis of the actual measurements to the first light densities, thereby obtaining a relative ratio matrix corresponding to arrangements of input and output portions of the object; and performs a matrix calculation by using the influence matrix and the

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relative ratio matrix, thereby obtaining feature data of the segments for reconstructing a tomographic image of the object.

In contrast, embodiments of the present invention, as now claimed, are directed to methods, systems, and computer-readable medium encoded with a computer program capable of determining an amount of at least one molecular specie comprising a sample, with each molecular specie being indicated by a dye, from an image of the sample captured as image data by a color image acquisition device, such as a color camera or an RGB camera, in a video-microscopy system. An optical density of the sample is first determined from the image data in each of a red, green, and blue channel at a pixel in the image so as to form a corresponding optical density matrix for the pixel. The optical density matrix is then multiplied by an inverse of a relative absorption coefficient matrix so as to form a resultant matrix for the pixel, wherein the relative absorption coefficient matrix comprises a relative absorption coefficient for each dye, independently of the sample, in each of the red, green, and blue channels. The resultant matrix thus comprising the amount of each molecular specie, as indicated by the respective dye, for the pixel.

I. Claims 1, 11, 14, 26-28, 36-38, 41, 42, 50-52, 55, 64-66, 72-74, 77, 78, and 86-88 Are Patentable

The Applicants have reviewed the rejections and submit that Claims 1, 11, 14, 26-28, 36-38, 41, 42, 50-52, 55, 64-66, 72-74, 77, 78, and 86-88 are patentable over the cited references for a variety of reasons, any one of which is sufficient to remove the rejections against the claims. It is Applicants' opinion that:

A. The Lundsgaard '769 and Ohta '617 patents, either separately or in combination, do not teach or suggest a system involving a color image acquisition device, a plurality of dyes for staining the sample, and the analysis of both sample and dye data in the red, green, and blue channels of the color image acquisition device; and

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B. A person of ordinary skill in the art would not have an objective reason for combining the teachings of the Lundsgaard '769 and Ohta '617 patents to arrive at the present invention as now claimed.

Each of these reasons is discussed more fully below.

A. **The Cited References Do Not Teach, Suggest or Provide Motivation for the Combination as Alleged in the Office Action**

The Applicants first note that the Federal Circuit has consistently stated that a finding of obviousness requires a specific teaching, motivation, or suggestion to combine the teachings of individual items of prior art. See, e.g., *In Re Sang Su Lee*, No. 00-1158 (Fed. Cir. January 18, 2002) (factual question of motivation to combine is material to patentability and could not be resolved on subjective belief and unknown authority); *C.R. Bard, Inc. v. M3 Systems, Inc.*, 157 F.3d 1340, 1352 (Fed. Cir. 1998) (a showing of a suggestion, teaching, or motivation to combine is an essential evidentiary component of an obviousness holding); *In re Fritch*, 972 F.2d 1260, 1265 (Fed. Cir. 1992) (Examiner can satisfy burden of obviousness in light of combination only by showing some objective teaching leading to the combination); and *In re Fine*, 837 F.2d 1071, 1075 (Fed. Cir. 1988) (evidence of teaching or suggestion essential to avoid hindsight).

In this regard, the Applicants also note that MPEP §2141 explicitly states that, when "applying 35 U.S.C. 103, the following tenets of patent law must be adhered to:

- (A) The claimed invention must be considered as a whole;
- (B) The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination;
- (C) The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and
- (D) Reasonable expectation of success is the standard with which obviousness is determined."

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Furthermore, in determining the differences between the prior art and the claims, “the question under 35 U.S.C. 103 is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious.” MPEP §2141.02, “Basic Considerations Which Apply to Obviousness Rejections,” *citing Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 218 USPQ 871 (Fed. Cir. 1983); *Schenk v. Nortron Corp.*, 713 F.2d 782, 218 USPQ 698 (Fed. Cir. 1983). (Emphasis added). The teaching or suggestion to make the claimed combination and reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. MPEP §2143 *citing In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). Also, “[t]he requirement “at the time the invention was made” is to avoid impermissible hindsight.” MPEP §2141.01(III). In addition, “[a] prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention.” *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984).

In light of these directives provided in the MPEP, the Applicants submit that separating background disclosure from each independent claim and then applying the cited references to the remainder, in the manner set forth in the Office Action, clearly does not consider each independent claim as a whole (i.e., the totality of the combination of elements, as recited). Furthermore, such rejections are entirely contrary to the requirement that the teaching or suggestion to make the claimed combination and reasonable expectation of success must both be found in the prior art, and not in applicant's disclosure. As such, the Applicants note that the Lundsgaard '760 patent is particularly directed to spectrophotometrically determining the concentration of a number of hemoglobin derivatives in whole blood and does not disclose a color image acquisition device having red, green, and blue channels from which an optical density of a sample stained with a dye for each molecular specie is determined at a pixel in an image of the stained sample. Further, the hemoglobin derivative samples that are the subject of the Lundsgaard '769 patent are not treated with any dye. That is, the Lundsgaard '769 patent does not disclose the use of any dye, much less determining a relative absorption coefficient matrix from a relative absorption coefficient for each of a plurality of dyes determined independently of the sample in each of the red, green, and

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blue channels of the color image acquisition device, as particularly claimed in the present invention.

Further, the Ohta '617 patent also cited in the Office Action is particularly directed to an optical computer tomographic apparatus for projecting light onto an object to be examined and reconstructing a tomographic image on the basis of the measurement value of the light transmitted through the object (as measured by a photodetector), and an image reconstruction method using optical computer tomography (CT) whereby a tomographic image is reconstructed in pseudocolor from the light intensities measured by the photodetector. The Ohta '617 patent further discloses that the "object" under consideration is a three-dimensional volume comprised of a plurality of volume elements (or "VOXELS"), whereby the image reconstruction method seeks to reconstruct a "slice" by considering the change in light transmissivity properties through a plurality of successive voxels. The Ohta '617 patent does not disclose a color image acquisition device having red, green, and blue channels from which an optical density of a sample stained with a dye for each molecular specie is determined at a pixel in an image of the stained sample. Further, the device disclosed by the Ohta '617 patent implements absorption coefficient values that are assumed under predetermined conditions for a measured CT volume element. As such, the relative absorption coefficient matrix determined, by assumption, by the Ohta '617 patent is not equivalent to determining a relative absorption coefficient matrix from a relative absorption coefficient for each of a plurality of dyes, independently of the sample, in each of the red, green, and blue channels of the color image acquisition device, as particularly claimed in the present invention.

The Applicants submit that the Lundsgaard '769 and Ohta '617 patents, either separately or in combination, clearly do not teach or suggest, whatsoever, a color image acquisition device having red, green, and blue channels from which an optical density of a sample stained with a dye for each molecular specie is determined at a pixel in an image of the stained sample. Further, the Lundsgaard '769 and Ohta '617 patents, either separately or in combination, clearly do not teach or suggest, whatsoever, determining a relative absorption coefficient matrix from a relative absorption coefficient for each of a plurality of dyes, independently of the sample, in each of the red, green, and blue channels of the color image acquisition device.

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acquisition device. That is, the Lundsgaard '769 and Ohta '617 patents do not, at all, involve a color image acquisition device having red, green, and blue channels for capturing an image of a sample, from which optical densities of the sample are determined. In addition, the Lundsgaard '769 and Ohta '617 patents do not, at all, involve a procedure whereby the color image acquisition device is used to determine a relative absorption coefficient matrix from a relative absorption coefficient for each of a plurality of dyes, independently of the sample, in each of the red, green, and blue channels. As such, any allegation in the Office Action that it would have been obvious to apply the teachings of the Lundsgaard '769 and Ohta '617 patents to a system involving a color image acquisition device, a plurality of dyes for staining the sample, and the analysis of both sample and dye data in the red, green, and blue channels of the color image acquisition device, must be finding motivation for the combination in the Applicants' disclosure. In this regard, the Applicants note that this is clearly admitted on Page 5 of the Office Action. Therefore, such an obviousness rejection is entirely contrary to the MPEP requirement that the teaching or suggestion to make the claimed combination and reasonable expectation of success must both be found in the prior art, and not in applicant's disclosure. As a result, each independent claim has not been considered as a whole, or a totality of a combination of recited elements, as also particularly required by the MPEP.

Thus, in view of these differences between embodiments of the present invention, as now particularly claimed in Claims 1, 14, 26, 41, 55, 64, and 77, and the Lundsgaard '769 and Ohta '617 patents, either separately or in combination, the Applicants submit that Claims 1, 11, 14, 26-28, 36-38, 41, 42, 50-52, 55, 64-66, 72-74, 77, 78, and 86-88 are patentable over the Lundsgaard '769 and Ohta '617 patents cited in the Office Action.

B. A Person of Ordinary Skill in the Art Would Not Have an Objective Reason for Combining the Teachings of the Cited References as Alleged in the Office Action

With respect to the person of ordinary skill in the art standard applied by the Office Action, it is particularly noted that "[t]here are three possible sources for a motivation to

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combine references: the nature of the problem to be solved, the teachings of the prior art, and the knowledge of persons of ordinary skill in the art." MPEP §2143.01, "The Prior Art Must Suggest the Desirability of the Claimed Invention," *citing In re Roussel*, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457-58 (Fed. Cir. 1998). In this regard, "It[the level of skill in the art cannot be relied upon to provide the suggestion to combine references." MPEP §2143.01, "The Prior Art Must Suggest the Desirability of the Claimed Invention," *citing Al-Site Corp. v. VSI Int'l Inc.*, 174 F.3d 1308, 50 USPQ2d 1161 (Fed. Cir. 1999). Furthermore, "[a] statement that modifications of the prior art to meet the claimed invention would have been "well within the ordinary skill of the art at the time the claimed invention was made" because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a prima facie case of obviousness without some objective reason to combine the teachings of the references." MPEP §2143.01, "Fact That the Claimed Invention is Within the Capabilities of One of Ordinary Skill in the Art is Not Sufficient by Itself to Establish *Prima Facie* Obviousness," *citing Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993); *In re Kotzab*, 217 F.3d 1365, 1371, 55 USPQ2d 1313, 1318 (Fed. Cir. 2000); and *Al-Site Corp. v. VSI Int'l Inc.*, 174 F.3d 1308, 50 USPQ2d 1161 (Fed. Cir. 1999).

With respect to the rejection of Claims 1, 14, 26, 41, 55, 64, and 77, the Office Action alleges that "[i]t would have been obvious for one skilled in the art, at the time the invention was made, to use Lambert-Beer's law as disclosed in Lundsgaard when processing the image data from each of the color channels in the applicant's admitted prior art as they both deal in finding concentrations of biological components in a specimen. This would result in improved identification of optical density of the sample and/or dye, thus providing motivation." The Applicants traverse this allegation, and thus traverse this rejection.

First, the application of the person of ordinary skill in the art standard in the Office Action to the obviousness rejection of Claims 1, 14, 26, 41, 55, 64, and 77 based upon the combination of the Lundsgaard '769 and Ohta '617 patents, as well as "the applicant's admitted prior art," is in direct contravention to MPEP §2143.01, which explicitly states that "It[the level of skill in the art cannot be relied upon to provide the suggestion to combine references."

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Further, as previously discussed, the Lundsgaard '769 and Ohta '617 patents, either separately or in combination, clearly do not teach or suggest, whatsoever, a color image acquisition device having red, green, and blue channels from which an optical density of a sample stained with a dye for each molecular specie is determined at a pixel in an image of the stained sample, or determining a relative absorption coefficient matrix from a relative absorption coefficient for each of a plurality of dyes, independently of the sample, in each of the red, green, and blue channels of the color image acquisition device. The motivation to combine alleged in the Office Action thus does not provide any objective reason as to why one having a system involving a color image acquisition device, a plurality of dyes for staining the sample, and the task of analyzing sample and dye data in the red, green, and blue channels of the color image acquisition device, would be motivated to use Lambert-Beer's law as disclosed in Lundsgaard and a relative absorption coefficient matrix in Lambert-Beer law calculations as disclosed in Ohta, when neither Lundsgaard nor Ohta teach or suggest such an application. As such, the alleged motivation to combine the Lundsgaard '769 and Ohta '617 patents is also in direct contravention to MPEP §2143.01, which explicitly states that the "[a] statement that modifications of the prior art to meet the claimed invention would have been "well within the ordinary skill of the art at the time the claimed invention was made" because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a prima facie case of obviousness without some objective reason to combine the teachings of the references."

Thus, in view of these factors, the Applicants further submit that Claims 1, 11, 14, 26-28, 36-38, 41, 42, 50-52, 55, 64-66, 72-74, 77, 78, and 86-88 are patentable over the Lundsgaard '769 and Ohta '617 patents cited in the Office Action.

II. Claims 2-10, 12, 13, 15-25, 29-35, 39, 40, 43-49, 53, 54, 56-63, 67-71, 75, 76, 79-85, 89, and 90

Claims 12, 13, 24, 25, 39, 40, 46, 53, 54, 68, 75, 76, 89, and 90 were also rejected in the Office Action as being obvious over the Lundsgaard '769 and Ohta '617 patents in view of U.S. Patent No. 5,734,498 to Krasieva *et al.* Claims 2-10, 15-23, 29-35, 43-49, 56-63, 67-71, and 79-

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85 were further rejected in the Office Action as being obvious over the Lundsgaard '769 and Ohta '617 patents in view of U.S. Patent No. 6,819,787 to Stone *et al.*

As previously discussed, Claim 1, upon which Claims 2-10, 12, and 13 depend; Claim 14, upon which Claims 15-25 depend; Claim 26, upon which Claims 29-35, 39, and 40 depend; Claim 41, upon which Claims 43-49, 53, and 54 depend; Claim 55, upon which Claims 56-63 depend; Claim 64, upon which Claims 67-71, 75, and 76 depend; and Claim 77, upon which Claims 79-85, 89, and 90 depend, are patentable over the Lundsgaard '769 and Ohta '617 patents. Thus, in response, the Applicant further submits that the present invention, as claimed in Claims 2-10, 12, 13, 15-25, 29-35, 39, 40, 43-49, 53, 54, 56-63, 67-71, 75, 76, 79-85, 89, and 90, is patentable over the Lundsgaard '769 and Ohta '617 patents. As such, the Applicant respectfully requests withdrawal of these rejections.

Conclusion

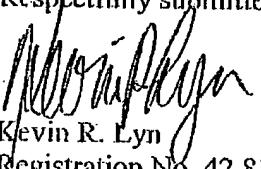
In summary, the Lundsgaard '769, Ohta '617, Krasieva '498, and Stone '787 patents, either separately or in combination, do not teach, suggest, or provide motivation for embodiments of the present invention, as now claimed in Claims 1, 14, 26, 41, 55, 64, and 77. Accordingly, in view of these differences between the Applicant's invention and the Lundsgaard '769, Ohta '617, Krasieva '498, and Stone '787 patents, it is submitted that the present invention, as defined by the pending claims, is patentable over the prior art cited in the Office Action. As such, Claims 1-90 are believed to be in condition for immediate allowance.

In conclusion, for the reasons set forth above, the Applicant submits that all claims now pending are in condition for immediate allowance. Accordingly, notice to such effect is respectfully requested at the Examiner's earliest opportunity.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

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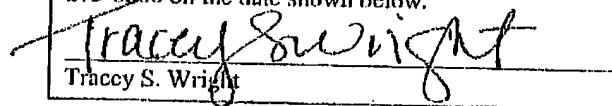
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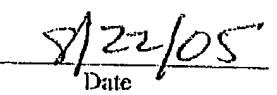

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